

Goulstonian Lectures

ON THE

CHEMICAL PATHOLOGY OF DIPHTHERIA
COMPARED WITH THAT OF ANTHRAX,
INFECTIVE ENDOCARDITIS, AND
TETANUS.

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LECTURE III.

THE specific action of the diphtheria products is brought into greater prominence when it is contrasted in parallel experiments with the chemical bodies found in anthrax and in infective endocarditis.

Infective endocarditis.—The case of infective endocarditis examined was under the care of Dr. Cayley at the Middlesex Hospital, and I performed the post-mortem examination when I was pathologist to that hospital. The history of the case may be briefly stated. The patient was a young unmarried woman, aged twenty-one years. The illness began eight weeks before death with pain in the left breast, and was characterised by wasting and intermittent fever during the six weeks' stay in the hospital. The temperature rose to 103° or 104° F. every day, and only once did shivering occur. The cardiac signs were those of double mitral disease. Four weeks before death the right brachial artery became plugged by an embolus, and three weeks before death the left femoral. Albuminuria occurred four weeks before death. At the post-mortem examination, twelve hours after death, there was chronic disease of the mitral valve, with fungating vegetation spreading over the endocardium of the left auricle, and ulcerated on the surface. The blood was imperfectly coagulated, and was lakey in colour. There was a recent embolus in the left middle cerebral artery, and older emboli (surrounded by organising thrombus) in the right brachial and left femoral arteries, while at the origin of the superior mesenteric artery there was a softening embolus. The right kidney showed two scars of old infarcts, and there were two caseated infarcts in the spleen. The spleen was greatly enlarged, dark, and congested. The liver was fatty, the kidneys fibro-fatty, and the lungs oedematous. This was, then, a case of ulcerative endocarditis not associated with abscesses or pyæmia. The mitral valve was examined microscopically and the blood and spleen chemically, while cultivations were made from the blood and from the vegetations on the mitral valve. Microscopically the mitral valve showed the fibrous thickening of chronic disease with recent vegetations capped by fibrin. A section of the free edge of the vegetations showed the fibrils of fibrin capping the thickened connective tissue containing collections of round cells. Along the free edge of the fibrin was a fringe of micrococci, very thick and invading the fibrin. Outlying clusters of the cocci were also present, and in some parts the micro-organisms were seen in groups in the tissue of the valve itself. In some parts of the valve the cocci were present in the valve tissue itself in the form of clusters. In this case, then, the micro-organism has for its culture medium the fibrin capping the vegetations.

Bacteriological examination.—No micro-organisms were found by making cultivations of the blood of the right ventricle. From the vegetations, with proper precautions, a pure cultivation was at once obtained of cocci with the same microscopical appearances as those seen in the valves—viz., they were cluster or staphylo-cocci, and not streptococci. Only one culture out of the five made showed any contamination; four were pure, and showed only the growth of the staphylococci. Without going further into the bac-

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teriological procedure, this organism may be described as growing on agar in bluish-white opaque circular colonies, and on gelatine in a similar manner, but rapidly liquefying the medium. Microscopically it is a staphylococcus, forming clusters and not chains.

Pathological action.—This coccus does not produce pus when introduced under the skin of a guinea-pig or into the circulation of a rabbit. In a guinea-pig it produces a febrile disorder lasting over eleven weeks, accompanied by extreme wasting and ending in death. When injected into the circulation only a slight illness results, from which the animal recovers. When killed, no micro-organisms were discovered in the blood. The pathological effects of this micro-organism have yet to be completely worked out. I contented myself as a commencement in determining what sort of illness it produced in animals and whether it formed abscesses. The kind of illness produced, and the absence of abscesses when subcutaneously introduced, showed that it had the characteristics of the coccus found in the valves of the heart. Each case of infective endocarditis must be studied by itself, for the disease is by no means an entity. Some cases of ulcerated cardiac vegetations occur as part of a pyæmia proceeding from pelvic or other abscesses, where the primary infective agent appears to be the staphylococcus or streptococcus pyogenes. In others, again, no primary pus focus is found, but there are multiple abscesses due to infective emboli from the ulcerated valves. Other organisms, such as Friedländer's pneumococcus, may also possibly play a part in the disease. In the case under consideration, however, there was only one micro-organism, and that one not a pus former.

Chemical examination.—A chemical examination was made of the blood and spleen by the same methods I have already described. The result showed that the same two classes of products are present in the blood and spleen as in anthrax and diphtheria—viz., digested proteids or albumoses, and a non-proteid product, which when first separated and purified is strongly acid. The albumoses are proto- and deuto-albumose, chiefly the latter, indistinguishable by chemical reactions from the similar bodies we have already discussed. The final product is separated by alcohol and purified by precipitation with ether and treating with chloroform. It is an amorphous, yellowish-brown body, with a strongly acid reaction. The amount of the products is seen in the following table:—

In Infective Endocarditis.

	Albumoses.	Alcoholic Extract.
From blood	0.236 gramme	Trace
From spleen	6.705 grammes	1.29
Total	6.941 grammes.	

The large amount of albumoses and alcoholic extract present in the spleen is remarkable. Here, again, as in diphtheria and anthrax, the spleen is the repository and manufactory of the chemical poison.

Physiological action of the albumoses.—The physiological action of the albumoses was tested side by side with that of anthrax albumoses while the experiments on diphtheria were progressing, so that the animals could be compared. The albumoses of infective endocarditis are producers of fever and retard the coagulation of the blood. The effect of the intravenous injection of a dose of 0.122 gramme per kilogramme of body weight is with the anthrax albumoses a great rise of temperature, lasting for three days; with the infective endocarditis albumoses the fever produced is much less marked. With a larger dose (0.2 gramme per kilogramme of body weight) the fever in the case of the anthrax albumoses is not so well marked; while in the case of the albumoses of infective endocarditis it is more marked than with the smaller dose. With a still larger dose (0.3 gramme) the anthrax albumoses cause only a slight rise of temperature, succeeded by a fall and death in two hours; while the albumoses of infective endocarditis cause a moderate rise of temperature, which is continued for two days. The anthrax albumoses, therefore, are much more toxic than those from infective endocarditis. The fever produced by them is well marked with a small dose, but with larger doses it is less, and with a lethal dose it is very slight indeed. In the experiments just described there is no paralysis produced, but wasting is observed in some of the animals.

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A Mirror OF HOSPITAL PRACTICE, BRITISH AND FOREIGN.

Nulla autem est alia pro certo noscendi via, nisi quamplurimas et morborum et dissectionum historias, tum aliorum tum proprias collectas habere, et inter se comparare.—MORGAGNI *De Sed. et Caus. Morb.*, lib. iv. Proœmium.

ROYAL FREE HOSPITAL.

CASE OF IMPACTION OF THE GILL-PLATE OF A HERRING
IN THE LARYNX OF AN INFANT; TRACHEOTOMY;
REMOVAL OF BONE; DIFFICULTY IN REMOVAL OF
TUBE FROM FUNCTIONAL PARALYSIS OF
ABDUCTORS; COMPLETE RECOVERY.

(Under the care of Dr. SAMUEL WEST.)

THIS case is interesting in two particulars: first, on account of the period of latency; and, secondly, because of the difficulty in the subsequent removal of the tube. The impaction of the bone in the larynx was marked by an initial attack of dyspnoea of great severity. The dyspnoea quickly subsided, and for four days continued so slight that no serious importance was attached to it. At the end of that time, however, it returned, and rapidly became urgent. The explanation is clear. The initial attack was due to the spasm set up, and the subsequent dyspnoea to the consecutive inflammation. The first was transitory and the second permanent. The difficulty in removing the tube was without doubt due to the closure of the glottis as the result of paralysis of the abductors, for the child could cry audibly though it could not inspire. The abductor paralysis was, Dr. West thought, the result of disuse, of laziness if we like to call it so, of the abductor muscles, and it was not until they had been roused to action again by the means used to dilate the glottis that they began to functionate.

Kate C—, a healthy infant aged nine months, was brought into the hospital suffering from considerable dyspnoea, with stridor and great recession of the chest walls. The movements of the larynx on respiration were greatly exaggerated. The face was pale and the child drowsy. The diagnosis was made of obstruction to the main air tube, in all probability in the larynx, and the history favoured the view that it was due to a laryngitis excited by a foreign body. The condition of the child was so serious that tracheotomy was performed at once, with immediate relief to the symptoms, after which the child went to sleep and slept comfortably the whole night. The mother stated that the child was perfectly well until the middle of the day on July 30th, 1889. It was then quite suddenly seized with urgent dyspnoea, and was thought to have swallowed a plum-stone. After a little while the urgency of the dyspnoea passed off, and, though the breathing continued short during the rest of that day and the next day, it was not bad enough to call in a doctor, and on the afternoon of the 31st the child was brought to the out-patient room, but, in spite of the history, was not thought to be a case for admission. The next day it was still better, and played about cheerfully all day; but at 10 o'clock in the evening the dyspnoea returned, and rapidly became worse, so that early on the morning of Aug. 2nd the child was brought to the hospital and admitted. When Dr. West saw it in the afternoon he advised instant tracheotomy. On the evening of the 2nd after the operation the temperature rose to 101.2°, and the next morning to 101.4°, and then fell gradually to below normal on the 5th, rising, however, the next day to 100.4°, but from this time it remained, with one or two exceptions, due to accidental causes, steadily below normal. The child progressed favourably till the morning of the 6th, when a severe attack of dyspnoea set in again suddenly. This lasted but a short time, and did not recur until midday, but lasted until Dr. West saw it about 3 o'clock. There was then considerable recession, and the child was cyanosed. The tube was removed, and after a violent fit of coughing a piece of the antiseptic gauze with which the wound had been dressed was coughed up. The dyspnoea still continuing, though not so severely, the air tubes were examined with a fine probe as far as could be done; and feeling something hard in the larynx above the wound, Dr. West introduced a pair of forceps, and removed a fishbone. The trachea was next examined and a curved wire passed down it in case there might be

any more of the gauze within reach, but none was detected. The removal of the bone did not at once greatly relieve the dyspnoea, but by the next morning the breathing was comparatively easy. In the evening of the 7th the tube was removed, and remained out for about an hour, but the respiration was carried on entirely through the wound. The tube was now left out every day for a short time, and frequently when the tube was out the child cried vigorously. Still it was evident that the air did not pass through the larynx, for after an hour or so, as soon as the granulations round the wound had had time to swell up and close the orifice, dyspnoea set in and the tube had to be replaced. On Aug. 19th it was found that the child was able to breathe for a little time through the larynx, but after this day it became more and more difficult to keep the tube out on account of the dyspnoea produced. On Sept. 5th the child was anaesthetised and a fresh examination made by Mr. Stabb. The tube was removed, and a graduated bougie (No. 11) was passed up through the larynx between the cords. It was then also passed from the mouth downwards through the larynx. The wound was then closed, but dyspnoea immediately returned. A dilator was then taken and passed between the cords, and the blades slightly separated. For a few seconds after this the patient was able to breathe through the mouth when the wound was closed, but dyspnoea again returned, and a silver tube was inserted in the wound. Nothing was felt which could explain the dyspnoea. On the 7th, when the tube was taken out, the breathing through the mouth was perfectly natural and continued so henceforth, so that the tube was not again inserted. The child continued well, and was discharged with the wound completely healed on the 18th. The bone which was removed was one of the gill-plates of a small fish, probably a herring.

MANCHESTER ROYAL INFIRMARY

MYXEDEMA TREATED BY THYROID GRAFTING.

(Under the care of Dr. THOMAS HARRIS and Mr. G. A. WRIGHT.)

IT is very advisable that this method of treating what has hitherto been an incurable disease should receive the fullest investigation, and cases in which it has been tried be reported. The grafts have been taken from other patients who were suffering from parenchymatous enlargement of the thyroid gland, which was producing symptoms for which it was considered advisable to remove part of the gland, also from sheep and from monkeys. Evidence of the good produced by this grafting when the grafts have retained their vitality and become vascularised is accumulating; but it is necessary to watch the patient for some time before satisfactory conclusions can be come to with regard to the benefit derived by any particular case. We have not space to consider the history of this method of treating myxœdema and allied conditions; the experiments and observations of Schiff, von Eiselsberg, Carle, and others are, however, not only interesting in themselves, but important in that they show the good effect on some of the lower animals, whilst the investigations of other observers prove that the good result of the grafting may be long continued if not permanent.

Mrs. T—, aged forty-eight, was admitted to the Royal Infirmary on March 6th, 1891. There was no family history of goitre or of myxœdema. The patient was a resident in Manchester, though she had travelled a good deal about the country. She was the mother of five children, three of whom are alive and well, two others died from convulsions during teething, and she had had two miscarriages. She gave the following history of her illness. She has been ailing more or less for nine years, when she suffered from a bad attack of bronchitis, and at this time she noticed that her neck was enlarged. The swelling was painted with iodine, but for a time increased until her neck became nearly twice as large as at the time of her admission; it attained its greatest size about eight years ago. She herself attributed the swelling to her persistent cough. The fullness of the neck then began gradually to subside, and she noticed that the ankles and abdomen occasionally swelled; frequency of micturition at night was also a new symptom. About two years and a half ago a still more severe attack of bronchitis came on, and the swelling of the feet and abdomen increased, and finally spread to her face. At this time the neck was nearly natural in size. It is with

the last two years and a half that the features of the present disease have developed, the most striking symptoms being a slowness of speech, swelling of the face, and weakness, together with a feeling of "strangeness" in the head, and a sensation of the mouth being smaller than natural. Such was the account obtained by the dresser on her admission. Mr. Deakin, surgical registrar, gives the following description of her condition at that time: "She is a fairly well nourished woman of forty-eight. The skin is dry and thick, but (with the exceptions to be presently mentioned) not hard or scurfy; it is in most cases of a yellowish earthy colour, but over the nose and to a certain extent over the cheeks it is dull reddish. The alae of the nose and the lips are red, smooth, and full, and no wrinkles are to be seen in any part of them. The eyebrows are very much elevated and perfectly uniformly so, and the forehead is marked with three or four lines, horizontal in the centre, and curving over towards the sides. These lines help much to give her the peculiar staring look she possesses. The conjunctivae are oedematous and glistening. The hair is fairly thick and strong. The mouth, gums, and palate are all rather oedematous. The tongue is markedly enlarged, somewhat pale, and its borders are indented. The eyelids are very markedly swollen and are pale and translucent, especially the lower, which show a distinct, soft, smooth pouch; the whole appearance resembles very closely that seen in chronic Bright's disease. The neck is flabby and soft, and examination of it gives the idea that some tough, hard, shrunken remains of the thyroid can be felt. The skin of the hands is dry, hard, thin, and scaly; the fingers are pointed; the nails are normal, but are overlapped by the skin, so that no groove can be made out. The hands are not unusually large. The abdomen is prominent around the umbilicus; there is no ascites; there is no oedema of the legs; the left limb is longer than the right; there is tenderness of both calves on pressure; the skin of the feet is horny and dry, and the toes are flattened together. The patient is fairly intelligent. Her sight has slowly been failing; her hearing is good; taste perhaps less distinct than it used to be. Pupils normal. Plantar, epigastric, and abdominal reflexes not obtainable; knee-jerk and deep reflexes over radius and olecranon are diminished. Sensation generally seems delayed; her speech is very markedly modified; and mastication and swallowing are slow. Pulse 60; heart normal. Appetite good; bowels regular. Respiration 17, a few râles occasionally. Urine 1010, acid, no sugar, contains a trace of albumen. The red blood-corpuscles were estimated at 5,970,000 per centimetre. No excess of white corpuscles. Haemoglobin nearly normal in amount."

The patient was kept in hospital, and chiefly in bed, for a month before operation. During that time her general condition improved considerably, and the swelling of the face was less marked; the speech and other conditions remained little altered. On April 4th a curved incision was made below each breast, and the glands were raised a little from the pectoral muscles. Half the thyroid gland of a small, young, green monkey, which was chloroformed to death in the ante-room of the theatre, was then placed under each breast. The wounds were closed and dressed. The operation wounds healed by primary union and without any disturbance, and the patient expressed herself as feeling better. On the 29th she was sent to the convalescent hospital, and her condition then was decidedly better than on admission. The improvement was maintained, and she was sent home after being in the country for some weeks. She relapsed very much into her former state under the less favourable surroundings of her home, and was readmitted to the infirmary very much as she was at first. She again immediately improved, but it is clear that the improvement is due far more to the wholesome circumstances of her hospital life than to any special treatment. Her speech is quite unaltered. She herself, however, is strongly of opinion that she is much improved.

Remarks by Dr. HARRIS and Mr. WRIGHT.—There is, we think, no doubt that this case is clearly one of myxoedema. The history of the affection of the thyroid causing first enlargement and subsequently complete or almost complete atrophy is interesting. The monkey's thyroid was exceedingly small, and though it set up no irritation in its new position, we were quite unable to say whether it remained as it was, was absorbed, or grew. At any rate, we could feel no trace of it afterwards. We fear the temporary improvement must be put down entirely to better hygienic conditions, and so far as the thyroid grafting goes, no conclusion can be drawn from this case.

ROTUNDA LYING-IN HOSPITAL, DUBLIN.

MATERNITY CASES.

(Under the care of Dr. JOHN H. GLENN, Assistant Master.)

THE accounts of these cases will be read with interest, as they give descriptions of unusual conditions. The complication of parturition referred to in the first case is luckily a very unusual one, and is not infrequently fatal. Two cases which somewhat resemble it have been recently described: one by Hirschfeld, in which the rupture extended through the cervical part of the uterus, and in which treatment similar to that followed by Dr. Glenn proved successful; another by Dr. Taylor, in which the rent extended through the posterior vaginal wall and was of large size, and which ended fatally in spite of antiseptic precautions. The necropsy does not afford any reason for regarding the hyperpyrexia as due to septic absorption.

CASE 1. Accidental hæmorrhage; rupture through posterior vaginal vault; recovery.—M. B.—, aged twenty-five, multipara, was admitted to the Rotunda Hospital in labour on the evening of Nov. 18th, 1891. Dr. Glenn was called to the case just after midnight on account of some slight ante-partum hæmorrhage. On palpation the child was made out lying in the first vertex position, the uterus was very tense, the lower segment greatly thinned, and the contraction being strongly marked. No foetal heart could be heard. The bladder was empty. The tenseness of the abdominal walls, the almost constant pain and the general condition all pointed to accidental hæmorrhage. On examination per vaginam the diagnosis was verified by a gush of blood following the pushing up of the head. Having disinfected the external parts, and douched the vagina with carbolic solution (1 in 40), internal version was performed, a foot brought down, and the case left to nature. Half an hour later, the hæmorrhage recurring, traction was made on the foot, and the delivery gradually completed. After the expulsion of the child, hæmorrhage continuing, and the patient looking very collapsed, an ineffectual attempt was made to express the placenta, which, however, was found to have left the uterus. It was removed from the vagina by hand, and at the same time a laceration of the cervix, extending backwards through the posterior vaginal vault, was made out, the arm passing upwards through the rent into the abdominal cavity as far as the elbow. A long strip of iodoform gauze was introduced through the rent, the lower end left in the vagina, a compress and binder applied, and restorative treatment employed. During the afternoon the patient was given a quarter of a grain of morphia hypodermically. The catheter was passed regularly. On the 23rd the plug was removed; no hæmorrhage followed. On the 27th the patient was deeply jaundiced. Her urine was examined for urobilin, but with a negative result. The yellow tinge gradually disappeared, and she made an uninterrupted recovery, the highest temperature being 99.8°. The patient was discharged from hospital on Dec. 18th, 1891.

CASE 2. Puerperal mania; hyperpyrexia; death.—M. D.—, aged twenty, unmarried, primipara, was admitted on Nov. 18th, 1891. Her state of health on admission was good, but she was suffering from considerable mental depression. On Nov. 20th, at midnight, the patient was delivered by forceps, as the temperature had risen to 101.2°. The os was almost fully dilated. No special difficulty was experienced, but the perineum was lacerated, requiring three stitches. The child was born alive. The following day the patient was very unruly, and got out of bed and took her binder off. Her evening temperature on the 23rd was 100.6°; the lochia normal. Nothing of special interest occurred till the 26th, when she was very restless, her face flushed, and with an expression of suspicion. Stitches were removed; the union was perfect. Her evening temperature was 98.6°. On the 27th she developed well-marked mania. Hyoscine ($\frac{1}{4}$ gr.) was given. Evening temperature 102°; pulse 103. Slept badly. The following day the patient was very violent. Bromide of potassium (30 gr.) was administered. Her skin was harsh and dry; wet pack given. Morning temperature 102°, evening 102.4°. On the 29th, at 6 A.M., she had a rigor, and half an hour later her temperature in the axilla was 109.4°. The temperature was verified by three certificated thermometers. Death took place at 7 A.M. Post-mortem examination by Dr. Earl revealed no cause for death; there was no meningitis, and the thoracic and abdominal organs were healthy.